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elf atochem

ATO

Elf Atochem North America, Inc.
2000 Market Street
Philadelphia, PA 19103-3222
Tel.: 215.419.7000

ORIGINAL

(A)

September 15, 1994

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8EHQ-94-12988
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Office of Pollution Prevention and Toxics
Environmental Protection Agency
401 M St. S.W.
Washington, D.C. 20460
Attn: Section 8(e) Coordinator

Contains No CBI

Subject: TSCA Section 8(e) Submission

Dear Sir/Madam:

Elf Atochem North America Inc. has recently received a final report from an acute inhalation toxicity study in rats and is submitting it to the Environmental Protection Agency (EPA) pursuant to Toxic Substances Control Act (TSCA) Section 8(e). Although this study was conducted in 1989 by Atochem in France, it has only just come into our possession. The study provides information on Thioglycolic acid (Mercaptoacetic acid, CAS No. 68-11-1) and does not involve effects in humans. The title of the enclosed study is Thioglycolic Acid Acute Inhalation Toxicity Study in Rats 4-Hour Exposure.

Nothing in this letter or the enclosed study report is considered confidential business information of Elf Atochem.

In this study, groups of 5 male and female rats were exposed by whole body exposure for 4-hours to aerosols of thioglycolic acid. The 4-hour LC_{50} was estimated to be 0.21 mg/l (210 mg/m^3). The ACGIH Threshold Limit Value (TLV-TWA) for thioglycolic acid is 1 ppm (3.8 mg/m^3), with a skin notation. The Elf Atochem MSDS for thioglycolic acid states to avoid skin and eye contact, and to avoid breathing fumes or vapors. The MSDS recommends personal protective equipment for eye, skin and the respiratory tract. The MSDS is currently being updated to include the information from the inhalation study.

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11/18/94

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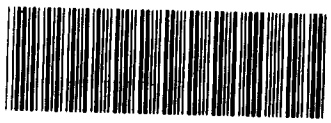

(2)

Elf Atochem has not previously filed any 8(e) notices or Premanufacture Notifications (PMNs) on the subject material. Further questions regarding this submission may be directed to me at (215) 419-5892.

Sincerely,

C.H. Farr, PhD, DABT
Manager, Product Safety
and Toxicology

Enclosure

[redacted]

ATO 39/881402

THIOGLYCOLIC ACID

ACUTE INHALATION TOXICITY

IN RATS

4-HOUR EXPOSURE

Contains No CBI

Sponsor:

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Usine de Laq,
64170 Artix.

Addressee:

Dr. Regnier,
Responsable des Etudes Toxicologie,
Atochem,
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92091 Paris la Defense,
FRANCE.

Report issued 13 January 1989.

Authors:

Graham C. Jackson,
Colin J. Hardy,
Rupanagudi S. Rao,
David J. Lewis,
Chirukandath Gopinath.

Huntingdon Research Centre Ltd.,
Huntingdon,
Cambridgeshire,
PE18 6ES,
ENGLAND.

TABLES

APPENDICES

(6)

Test substance: A clear, colourless liquid identified as THIOGLYCOLIC ACID.

Test animals: Albino rats, (WISTAR). One control group and 4 test groups each of 5 male and 5 female rats.

Route of administration: By inhalation of a test atmosphere containing a liquid droplet aerosol generated from the test substance.

Duration of exposure: 4 hours continuous whole-body exposure.

Observation period: 14 days post exposure.

Results

Exposure levels and mortality:

Level (mg/l)	Mortality Males	Females	Total
0.068	0/5	0/5	0/10
0.172	2/5	2/5	4/10
0.338	3/5	4/5	7/10
0.582	5/5	5/5	10/10

Clinical signs:

(a) During exposure: signs consistent with exposure to an irritant aerosol including, partial closing of the eyes, wetness around the eyes and around the mouth, abnormal respiration, restless behaviour and the adoption of a hunched posture.

(b) During observation period: signs seen in rats exposed to THIOGLYCOLIC ACID included abnormal respiration, brown staining around the snout and jaws and sensitivity to touch.

Recovery from the effects of the exposure, as determined by the appearance and behaviour of the rats, was complete by 3 to 13 days post exposure, depending on the exposure level.

Bodyweight:	Reduced bodyweight or rate of bodyweight gain, related to the exposure level, for up to 3 days following exposure. Subsequently weight gain was similar to that for control rats.
Food and water consumption:	Food consumption was reduced for 1 day in male rats and for up to 4 days in female rats following exposure to THIOGLYCOLIC ACID at 0.172 or 0.338 mg/l. Water consumption was reduced for up to 2 days in male rats exposed at 0.172 or 0.338 mg/l and for 3 days in female rats following exposure at 0.338 mg/l.
Lung weight to bodyweight ratio:	The lung weight to bodyweight ratios for most rats that died as a result of exposure were high. The lung weights for rats that survived exposure to THIOGLYCOLIC ACID were generally within normal limits but higher than expected in a proportion of rats exposed at 0.068 mg/l.
Estimation of the LC_{50} (4-hour):	The LC_{50} (4-hour) for THIOGLYCOLIC ACID is estimated at 0.21 mg/l of air. The standard error of the estimate is 0.040 mg/l.
Macroscopic pathology:	The lungs of the majority of rats that died as a result of exposure were congested. There were no macroscopic abnormalities in rats that survived exposure to THIOGLYCOLIC ACID and no abnormalities in the control rats.
Microscopic pathology:	The lungs of rats that died as a result of exposure were congested. There were no other treatment-related findings.

The acute inhalation toxicity of THIOGLYCOLIC ACID was assessed by exposing 4 groups of rats each for a period of 4 hours to aerosols produced from the test substance.

The study was conducted at the Huntingdon Research Centre during the period 18 May 1988 to 16 June 1988.

The protocol for the study was approved by the Study Director and HRC Management on 15 February 1988 and approved by the Sponsor on 7 March 1988.

On completion of the study all data relating to the study, including preserved tissues and a copy of the final report, were lodged in the Huntingdon Research Centre Archives, Huntingdon, Cambridgeshire, England.

Test substance

The test substance was a clear colourless liquid identified as:

ACIDE THIOGLYCOLIQUE (THIOGLYCOLIC ACID)
Reference 6218

The sample was received on 17 February 1988 and was stored in the dark at 4°C and in the original container.

The data supplied by the Sponsor indicated that the test substance was adequately stable for use in this study.

The test substance is referred to as THIOGLYCOLIC ACID in this report.

Animals and maintenance

Twenty-five male and 25 female albino rats (Wistar), about 6 weeks and 8 weeks old respectively, were obtained from Charles River UK Limited, Manston Road, Margate, Kent, England. The rats were obtained in 2 batches. The first batch (20 male and 20 female) was received on 18 May 1988 and the second batch (5 male and 5 female) was received on 25 May 1988. The ages of rats were selected so that males and females would be of similar bodyweight (ca. 200g) on the day of exposure.

On arrival the rats were allocated to 1 of 5 groups, each of 5 males and 5 females and were identified individually by a number tattooed on the ears. The rats were housed 5 of like sex to a cage and acclimatised to laboratory conditions for at least 5 days before the day of exposure.

The cages were made of polypropylene (size 38 cm x 56 cm x 18 cm height) and had detachable wire mesh tops and floors. The cages were suspended on a movable rack. While in their cages all rats had free access to a measured excess amount of food (Labsure LAD 1) and tap water. Food and water supplies were analysed routinely to determine the levels of chemical or microbiological contaminants.

The rats remained in a holding room except for the 4-hour exposure and an overnight post exposure period when the rats exposed to THIOGLYCOLIC ACID were kept in a ventilated cabinet to allow dispersal of any residual test substance.

The mean daily maximum and minimum temperatures of the holding area during the study are shown below:

Groups	Dates	Mean maximum temperature (°C)	Mean minimum temperature (°C)	Mean RH (%)
1 - 5	18.5.88 - 16.6.88	22 (0.7)	20 (0.5)	55 (6.6)

The numbers in parentheses are the standard deviations of the mean.

Inhalation exposures

Four groups of rats were exposed continuously for 4 hours to test atmospheres containing a liquid droplet aerosol generated from THIOGLYCOLIC ACID. Each group was exposed to a different concentration of the test substance.

A further group acting as a control received clean air only for 4 hours.

The group identifications and dates of exposure for the groups were:

Group 1	(Control)	:	24 May 1988
Group 2	(Test)	:	24 May 1988
Group 3	(Test)	:	26 May 1988
Group 4	(Test)	:	27 May 1988
Group 5	(Test)	:	2 June 1988

The mean concentrations of the test aerosol for each group are given in the 'Results' section of this report.

Exposure system

Aerosol generator

The aerosol generator, shown in Figure 1, was designed to produce and maintain an atmosphere containing a high proportion of respirable droplets. All parts of the generator in contact with the test substance were made of stainless steel or glass.

The test substance was supplied to the generator from a syringe driven at a constant rate by a syringe pump. The compressed air supply to the generator was dried, filtered and oil-free.

Exposure chambers

The whole-body exposure chambers used for the exposures were of square section and were fitted with pyramidal tops. The chambers were made of perspex and had an internal volume of approximately 120 litres. Each chamber was divided by wire mesh partitions to provide 10 separate animal compartments.

The test atmosphere entered through a port at the base centre of the chamber and passed out through small holes in the lower edge of the square section. Each chamber was positioned inside a large cabinet equipped with an extract fan exhausting to atmosphere through a carbon-filled drum.

The exposure system is shown in Figure 2.

Procedure

A supply of clean dried air was connected to the aerosol generator and the supply pressure was adjusted to give a flow rate of 30 litres per minute measured at the generator outlet tube. An in-line flow meter was used to monitor air flow throughout the exposure.

A syringe filled with the test substance was fitted to the syringe pump and connected to the generator with PTFE tubing. A flow rate of 0.2 ml/minute was selected for the exposure of the first test group.

The rats to be exposed were placed into separate compartments of the exposure chamber.

The syringe pump was switched on and the exposure timed for 4 hours, following a 11-minute([1]) equilibration period, from the appearance of an aerosol from the generator outlet.

After 4 hours the supply of test substance was discontinued and the exposure chamber was allowed to clear before the rats were removed for examination.

The procedure was repeated, with appropriate flow rates of THIOGLYCOLIC ACID for each of the other test groups. The equilibration period for these groups was 9 minutes([1]).

The control group was treated similarly but exposed to air only.

Following exposure the rats were returned to the holding cages and food and water supplies were restored. The control rats were returned to the holding room. The rats exposed to THIOGLYCOLIC ACID were kept in a ventilated cabinet overnight and then returned to the holding room for the remainder of the observation period.

Chamber atmosphere analyses

Five air samples were taken from the chamber during each exposure and the collected material was analysed to determine the concentration of THIOGLYCOLIC ACID in the chamber air.

Each air sample was withdrawn, at 2 litres per minute, through a gas absorption trap (sintered glass bubbler) containing dichloroethane as the absorbant.

The trap was cooled to -70°C (cardice/acetone) before sampling and the volume of the air sample was measured with a wet-type gas meter.

([1]) 11 minutes is the theoretical time required for the concentration of aerosol in the chamber to reach 90% of its final value at an air flow rate of 25 litres per minute. At 30 litres per minute the equilibration period required is 9 minutes. The additional 2 minutes exposure received by the first test group (Group 2) was considered unlikely to have influenced the results of the study

Two additional air samples were taken during each exposure using a May multistage liquid impinger([1]) with dichloroethane as the trapping agent in each stage. The samples were taken approximately 1.5 and 3.5 hours after the start of exposure.

The contents of the stages of the sampler were analysed to determine the size distribution of THIOGLYCOLIC ACID droplets in the test atmospheres.

The collection characteristics for the sampler used at a sampling rate of 10 litres per minute are:

Stage 1 - particles greater than 5.5 μm aerodynamic diameter (a.d.)

Stage 2 - particles between 5.5 μm and 2.0 μm a.d.

Stage 3 - particles less than 2.0 μm a.d.

The method of analysis for THIOGLYCOLIC ACID is described in Appendix 1.

Chamber air temperature

The air temperature in the exposure chamber was measured with a mercury-in-glass thermometer and recorded at the start of exposure and then at 30-minute intervals during the 4-hour exposure.

Observations

Clinical signs

The rats were observed continuously for signs of reaction to the test substance during exposure and at least twice daily throughout the observation period.

Bodyweight

All rats were weighed daily from the day of delivery to the Huntingdon Research Centre until the end of the observation period.

Food and water consumption

The amount of food and water consumed by each cage of rats was measured daily from the day following arrival. The daily mean intakes of food and water for each rat were calculated from the recorded data.

([1]) May, K.R., Bacteriological Reviews 30, 3, 1966, pp 559-570.

Terminal studies

At the end of the 14-day observation period, the surviving rats were anaesthetised by intraperitoneal injection of pentobarbitone sodium and killed by exsanguination.

All rats that died as a result of exposure and those killed at the end of the observation period were subjected to a detailed macroscopic examination. The lungs were removed, dissected clear of surrounding tissue and weighed in order to calculate the lung weight to bodyweight ratio.

The lungs were infused with, and preserved in, buffered 10% formalin together with samples of the liver and kidneys for microscopic examination.

The fixed tissues were embedded in paraffin wax and processed routinely. Four-micron sections were prepared, stained with haematoxylin and eosin and examined under the light microscope.

Estimation of the LC_{50} (4-hour) and standard error

The concentration of the test substance likely to cause death in 50% of exposed rats following a single 4-hour exposure was calculated by the log probit method of Miller and Tainter([1]).

The standard error was calculated from the formula:

$$\text{SE of } LC_{50} = \sqrt{\frac{2s}{2N}}$$

where 2s is the estimated increment in concentration of the test substance between probits 4.0 and 6.0 corresponding to 16% and 84% mortality and N is the total number of rats in groups with mortality between 6.7% and 93.3% (Probits 3.5 - 6.5).

([1]) Miller, L.C. and Tainter, M.L., Proc. Soc. Exp. Bio. Med. 57, (2), 1944, pp 261-264.

CHAMBER ATMOSPHERE CONDITIONS

Concentration of THIOGLYCOLIC ACID

The analysis results for the air samples taken during the exposures are shown in Table 1.

The mean concentrations of THIOGLYCOLIC ACID in the chamber air and the variations in concentration (range x 100/mean) for each group were:

Group	THIOGLYCOLIC ACID in air (mg/l)	Variation (%)	Relative standard deviation (%)
2	0.582	53	21
3	0.172	116	48
4	0.068	134	53
5	0.338	56	22

The variations in concentration were much higher than expected and were considered to be related to the properties of the test substance. The aerosolisation process was inefficient, with average efficiences (analysed concentration x 100/nominal concentration) of 4 - 6%, due to the viscosity of the test substance and the observed variation may be associated with temperature dependent changes in viscosity during the exposure.

However, we consider that the mean analysed concentrations provide a good estimate of the exposure levels and that the variation would not have affected the mortality following exposure to THIOGLYCOLIC ACID.

Particle size distribution

The results for the air samples taken for determination of the particle size distribution of THIOGLYCOLIC ACID are shown in Table 2.

The results show that 76 - 89% of the THIOGLYCOLIC ACID present in the chamber atmosphere was in the form of particles of respirable size (<5.5 μm aerodynamic diameter).

Chamber air temperature

The mean chamber air temperatures and the standard deviation of the means, during exposure of the groups were:

Group	Temperature (°C) Mean	SD
1 (Control)	24.0	0.00
2 (0.582 mg/l)	24.8	0.44
3 (0.172 mg/l)	23.3	1.00
4 (0.068 mg/l)	22.7	0.50
5 (0.338 mg/l)	22.0	0.00

SD Standard deviation

There were no differences in temperature considered likely to influence the results of the study.

CLINICAL OBSERVATIONS

Mortality

The mortality is summarised below:

Group	Deaths		
	Male	Female	Total
1 (Control)	0/5	0/5	0/10
2 (0.582 mg/l)	5/5	5/5	10/10
3 (0.172 mg/l)	2/5	2/5	4/10
4 (0.068 mg/l)	0/5	0/5	0/10
5 (0.338 mg/l)	3/5	4/5	7/10

In Group 2 (0.582 mg/l) 5 male rats and 3 female rats died overnight following exposure. Two female rats were killed for humane reasons on Day 1 of the observation period.

In Group 3 (0.172 mg/l) 2 male rats and 2 female rats died overnight following exposure.

In Group 5 (0.338 mg/l) 3 male rats and 4 female rats died overnight following exposure.

Clinical signs

(a) During the exposure

The incidence of clinical signs observed during exposure is shown in Table 3. The signs seen during exposure were considered to be consistent with inhalation of an irritant aerosol and included partial closing of the eyes, an irregular respiration rate, adoption of a hunched body posture, wetness (probable lacrimation) around the eyes, wet fur, due to salivation, around the snout and jaws and restless behaviour.

(b) During the observation period

The incidence of clinical signs seen during the observation period is shown in Table 4. Column 0 of this table shows the observations made when the rats were removed from the exposure chamber. At this time signs evident in rats exposed to THIOGLYCOLIC ACID at 0.172 mg/l, or higher levels included wet fur around the snout, jaws and eyes, brown staining around the snout and jaws, abnormal breathing and hyperactivity. Later some of these rats were observed to be lethargic. In rats exposed at 0.068 mg/l only brown staining and wet fur were observed.

The rats that survived exposure showed brown staining around the snout and jaws for between 2 days in rats exposed at 0.068 mg/l and up to 10 days in rats exposed at 0.338 mg/l. Other signs observed were lethargy, sensitivity to touch, wet fur, the adoption of a hunched posture, diarrhoea, ataxia and abnormal breathing. Recovery from the effects of exposure, as judged by the appearance and behaviour of the rats, was complete within 3 days in rats exposed at 0.068 mg/l and within 13 days in rats exposed at 0.338 mg/l.

Bodyweight

The group mean and individual bodyweights are shown in Table 5.

There were decreases of bodyweight or reductions in the rate of bodyweight gain, related to the exposure level, for up to 3 days following exposure. Subsequently weight gain for rats that survived exposure to THIOGLYCOLIC ACID was similar to that of the control rats.

Food consumption

The food consumption data are presented in Table 6.

Food consumption was reduced for 1 day in male rats and for up to 4 days in female rats following exposure to THIOGLYCOLIC ACID at 0.172 or 0.338 mg/l. Slight reductions in food consumption were observed following exposure at 0.068 mg/l.

Water consumption

The water consumption data are presented in Table 7. Water consumption was reduced for up to 2 days in male rats exposed at 0.172 or 0.338 mg/l and for 3 days in female rats following exposure to THIOGLYCOLIC ACID at 0.338 mg/l.

TERMINAL STUDIES

Lung weight to bodyweight ratio

The lung weight to bodyweight ratio for individual rats is shown in Table 8.

The lung weight to bodyweight ratio was increased, due to a high lung weight, in most rats that died as a result of exposure to THIOGLYCOLIC ACID. The lung weights were generally within normal limits for the control rats and for the rats that survived exposure to THIOGLYCOLIC ACID but higher than expected in a proportion of rats exposed at 0.068 mg/l.

Estimation of the LC_{50} (4-hour) for THIOGLYCOLIC ACID

From the mortality data for Groups 2, 3, 4 and 5 the LC_{50} (4-hour) for THIOGLYCOLIC ACID was established at:

0.21 mg per litre of air (210 mg/m^3)

The standard error of the estimate was 0.040 mg/l.

Macroscopic pathology

The macroscopic pathological findings for individual rats are included in Appendix 2.

The findings for rats that died as a result of exposure to THIOGLYCOLIC ACID were typified by congestion of the lungs.

There were no treatment-related macroscopic abnormalities in rats that survived exposure to THIOGLYCOLIC ACID and no abnormalities in the control rats.

Microscopic pathology

The histopathological findings observed in the tissues examined are given in detail in Appendix 2.

The following comments are made in summary:

Decedent rats

Congestion in the lungs of decedent rats from groups receiving 0.582, 0.338 and 0.172 mg/L.

Animals examined at termination

No treatment-related changes were detected.

Incidental findings

All other findings observed were considered spontaneous in origin and therefore no toxicological significance.

FIGURE 1

Aerosol generator

a. Glass elutriating column.
b. Compressed air supply.
c, Feed tube with adjustment screw.
d. Venturi atomising jet.
e. Drain tubes.

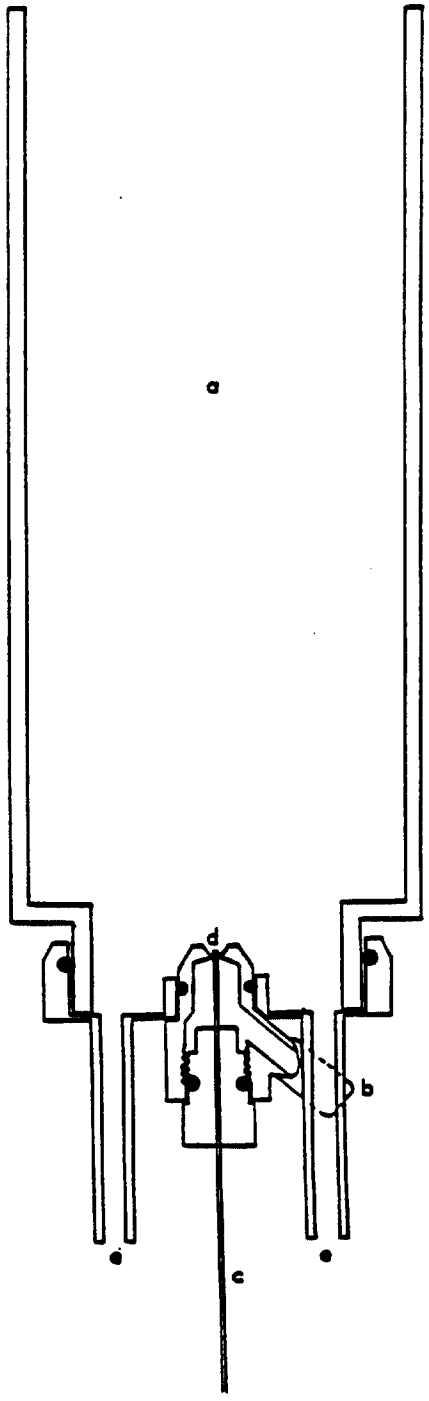
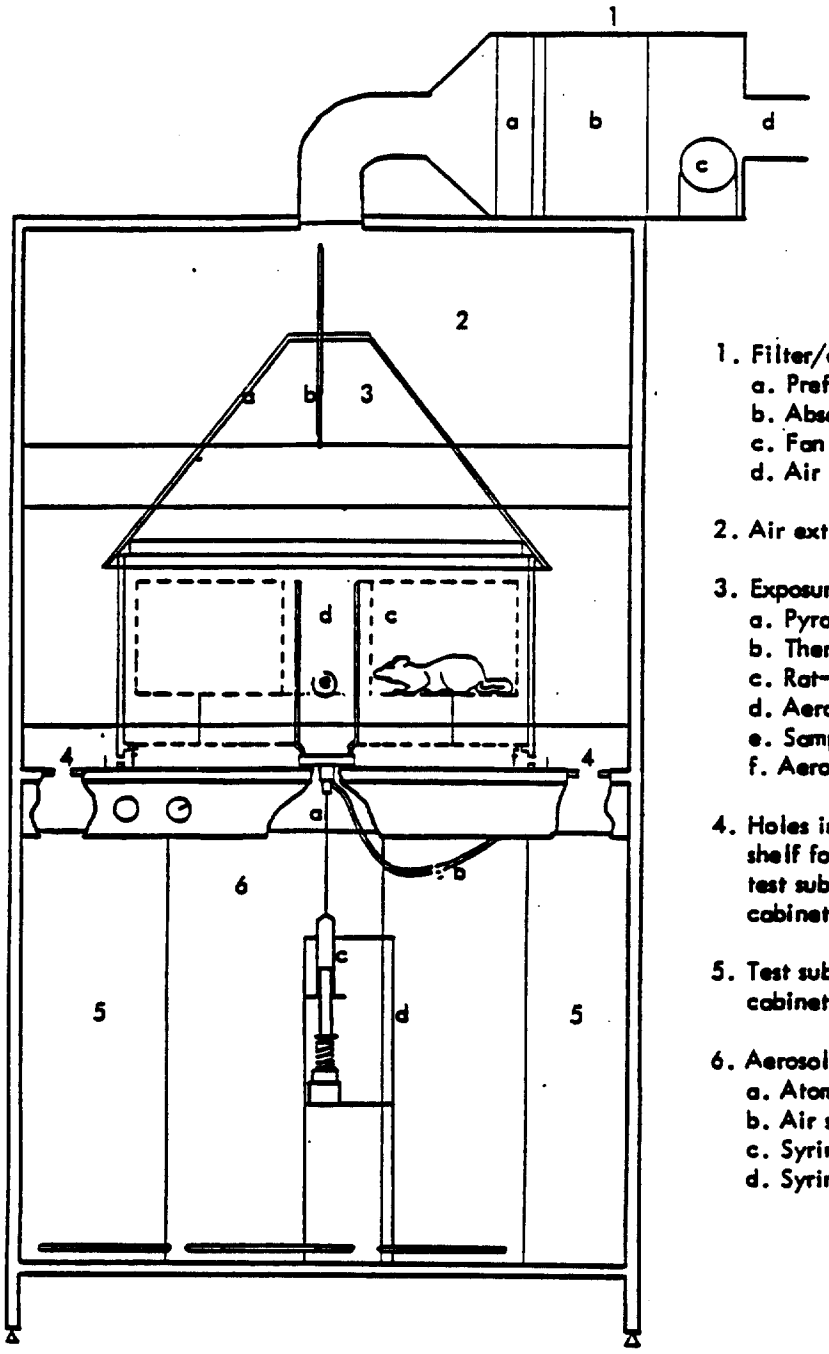


FIGURE 2

Exposure system



1. Filter/extract unit
   a. Prefilter
   b. Absolute filter
   c. Fan
   d. Air exit

2. Air extraction cabinet

3. Exposure chamber
   a. Pyramidal top
   b. Thermometer
   c. Rat-holding cage
   d. Aerosol entry column
   e. Sampling port
   f. Aerosol exit holes

4. Holes in chamber support shelf for air extract from test substance handling cabinet.

5. Test substance handling cabinet.

6. Aerosol generation system
   a. Atomiser
   b. Air supply
   c. Syringe
   d. Syringe pump

TABLE 1

Concentrations of THIOGLYCOLIC ACID

Group	Sample	Time	Amount in air (mg/l)	Variation (note a)
2	2.1	0h : 30m	0.700	
	2.2	1h : 00m	0.394	
	2.3	2h : 00m	0.675	
	2.4	3h : 00m	0.527	
	2.5	3h : 50m	0.613	
		Mean	0.582	53%
3	3.1	0h : 30m	0.110	
	3.2	1h : 00m	0.109	
	3.3	2h : 00m	0.171	
	3.4	3h : 00m	0.160	
	3.5	3h : 50m	0.309	
		Mean	0.172	116%
4	4.1	0h : 30m	0.023	
	4.2	1h : 00m	0.047	
	4.3	2h : 00m	0.063	
	4.4	3h : 00m	0.095	
	4.5	3h : 50m	0.114	
		Mean	0.068	134%
5	5.1	0h : 40m	0.239	
	5.2	1h : 30m	0.291	
	5.3	2h : 30m	0.356	
	5.4	3h : 00m	0.377	
	5.5	3h : 45m	0.428	
		Mean	0.338	56%

(a) Variation = range of values x 100/mean

TABLE 2

Particle size distribution of THIOGLYCOLIC ACID

Group	Sample	Time taken	Stage	Particle size range (μm)	Amount collected (mg)	% of total	% respirable	Mean % respirable
2	PSD 1	1h : 30m	1	>5.5	0.794	13.6		
			2	2.0-5.5	1.363	23.3		
			3	<2.0	3.688	63.1		
				Totals	5.845	100.0	86.4	
	PSD 2	3h : 30m	1	>5.5	0.431	9.0		
			2	2.0-5.5	0.475	9.9		
			3	<2.0	3.888	81.1		
				Totals	4.794	100.0	91.0	88.7
3	PSD 1	1h : 30m	1	>5.5	0.950	18.4		
			2	2.0-5.5	0.813	15.7		
			3	<2.0	3.400	65.9		
				Totals	5.163	100.0	81.6	
	PSD 2	3h : 30m	1	>5.5	0.456	23.5		
			2	2.0-5.5	0.369	19.0		
			3	<2.0	1.113	57.4		
				Totals	1.938	99.9	76.5	79.1
4	PSD 1	1h : 30m	1	>5.5	0.131	14.7		
			2	2.0-5.5	0.188	21.0		
			3	<2.0	0.575	64.3		
				Totals	0.894	100.0	85.3	
	PSD 2	3h : 30m	1	>5.5	0.706	34.2		
			2	2.0-5.5	0.606	29.4		
			3	<2.0	0.750	36.4		
				Totals	2.062	100.0	65.8	75.6
5	PSD 1	2h : 00m	1	>5.5	1.725	24.9		
			2	2.0-5.5	2.138	30.9		
			3	<2.0	3.063	44.2		
				Totals	6.926	100.0	75.1	
	PSD 2	3h : 30m	1	>5.5	2.488	21.3		
			2	2.0-5.5	2.156	18.5		
			3	<2.0	7.013	60.2		
				Totals	11.657	100.0	78.7	76.9

TABLE 3

Clinical signs during exposure

Group	Signs	Number showing signs						
		Time in hours						
		0*	0.25	0.5	1.0	2.0	3.0	4.0
1♂ (Control)	Normal appearance and behaviour	5	5	5	5	5	5	5
1♀ (Control)	Normal appearance and behaviour	5	5	5	5	5	5	5
2♂ (0.582 mg/l)	Wet fur						5	5
	Wet around the eyes				5	5	5	5
	Eyes partially closed		5	5	5	5	5	5
	Wet around snout			5	5	5	5	5
	Wet around mouth				5	5	5	5
	Irregular respiration				5	5	5	5
	Hunched posture		5	5	5	5	5	5
	Restless behaviour	5						
2♀ (0.582 mg/l)	Wet fur						5	5
	Wet around the eyes				5	5	5	5
	Eyes partially closed		5	5	5	5	5	5
	Wet around snout			5	5	5	5	5
	Wet around mouth				5	5	5	5
	Irregular respiration				5	5	5	5
	Hunched posture		5	5	5	5	5	5
	Restless behaviour	5						
3♂ (0.172 mg/l)	Eyes partially closed		5	5	5	5	5	5
	Wet around mouth			1	2	5	5	5
	Irregular respiration		5	5	5	5	5	5
	Hunched posture		5	5	5			
	Restless behaviour	5				5	5	5
	Pawing of cage mesh						4	5
3♀ (0.172 mg/l)	Eyes partially closed		5	5	5	5	5	5
	Wet around mouth				2	5	5	5
	Irregular respiration		5	5	5	5	5	5
	Hunched posture		5	5	2	1		1
	Restless behaviour	5			3	4	5	4
	Pawing of cage mesh						1	2

* Signs recorded during the equilibration period

TABLE 3

(Clinical signs during exposure - continued)

Group	Signs	Number showing signs						
		Time in hours						
		0*	0.25	0.5	1.0	2.0	3.0	4.0
4♂ (0.068 mg/l)	Restless behaviour	5	1					
	Eyes partially closed		5	5	5	5	5	5
	Hunched posture		4	5	5	5	5	5
4♀ (0.068 mg/l)	Restless behaviour	5	2	2	2			
	Eyes partially closed		5	5	5	5	5	5
	Hunched posture		3	3	3	5	5	5
5♂ (0.338 mg/l)	Normal appearance and behaviour	5	2					
	Eyes partially closed				5	5	5	5
	Wet fur around snout			5	5	5	5	5
	Irregular respiration		2	5	5	5	5	5
	Hunched posture		1	5	5	5	5	5
	Restless behaviour		2					
5♀ (0.338 mg/l)	Normal appearance and behaviour	5	1					
	Eyes partially closed				5	5	5	5
	Wet fur around snout			5	5	5	5	5
	Irregular respiration		4	5	5	5	5	5
	Hunched posture		1	5	5	5	5	5
	Restless behaviour		3					

* Signs recorded during the equilibration period

TABLE 4

Clinical signs during observation period

Group	Signs	Number showing signs														
		Day of observation period														
		0*	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1♂ (Control)	Normal appearance and behaviour	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
1♀ (Control)	Normal appearance and behaviour	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
2♂ (0.582 mg/l)	Wet fur on snout, jaws, head and around eyes	5														
	Matted fur	5														
	Hyperactive	5														
	Lethargic	5a														
	Dead (total)		5	5	5	5	5	5	5	5	5	5	5	5	5	5
2♀ (0.582 mg/l)	Wet fur on snout, jaws, head and around eyes	5	2													
	Matted fur	5	2													
	Hyperactive	5														
	Lethargic	5a														
	Immobile	2a														
	Dead (total)		5b	5	5	5	5	5	5	5	5	5	5	5	5	5

* Signs recorded after exposure on the day of exposure
a These signs were recorded at the late afternoon check
b Total includes 2 rats that died after the clinical signs had been recorded

TABLE 4

(Clinical signs during observation period - continued)

Group	Signs	Number showing signs													
		Day of observation period													
		0*	1	2	3	4	5	6	7	8	9	10	11	12	13	14
3♂ (0.172 mg/l)	Normal appearance and behaviour					2	2	3	3	3	3	3	3	3	3	3
	Hyperactive	5														
	Brown staining around snout and/or jaws	5	5	3	3	1	1									
	Wet fur around snout, jaws and eyes	5	1													
	Lethargic	1	1													
	Sensitive to touch		1													
	Increased respiration rate			3	3											
	Dead (total)		2a	2	2	2	2	2	2	2	2	2	2	2	2	2
3♀ (0.172 mg/l)	Normal appearance and behaviour					2	3	3	3	3	3	3	3	3	3	3
	Hyperactive	5														
	Crusty brown staining around snout, jaws and eyes	5	5	3	3	1										
	Wet fur around snout, jaws and eyes	5	5													
	Sensitive to touch		5													
	Increased respiration rate			3	3											
	Dead (total)		2	2	2	2	2	2	2	2	2	2	2	2	2	2
4♂ (0.068 mg/l)	Normal appearance and behaviour				5	5	5	5	5	5	5	5	5	5	5	5
	Brown staining around snout and/or jaws	5	5	5												
	Wet fur around snout, jaws and eyes	5														
4♀ (0.068 mg/l)	Normal appearance and behaviour				5	5	5	5	5	5	5	5	5	5	5	5
	Brown staining around snout and/or jaws	5	5	5												
	Wet fur around snout, jaws and eyes	5														

* Signs recorded after exposure on the day of exposure

a These rats died after the clinical signs had been recorded

TABLE 4

(Clinical signs during observation period - continued)

Group	Signs	Number showing signs														
		Day of observation period														
		0*	1	2	3	4	5	6	7	8	9	10	11	12	13	14
5♂ (0.338 mg/l)	Normal appearance and behaviour														2	2
	Brown staining around snout and/or jaws	5	2	2	2	2	2	2	2	2	2					
	Wet fur	5	2													
	Irregular respiration	5	2	2	2											
	Hyperactive	5														
	Lethargic	5a	2	2	2											
	Exaggerated respiratory movements					2	2	2	2	2	2	2	2	2		
	Dead (total)		3	3	3	3	3	3	3	3	3	3	3	3	3	3
5♀ (0.338 mg/l)	Normal appearance and behaviour														1	1
	Brown staining around snout and/or jaws	5	1	1	1	1	1	1	1	1	1	1				
	Wet fur	5	1													
	Irregular respiration	5	1	1	1	1	1	1	1	1	1	1	1	1		
	Hyperactive	5														
	Ataxia	1	1	1	1	1	1	1	1							
	Lethargic	5a	1	1	1	1										
	Yellow staining around urogenital area			1	1	1	1	1	1	1	1	1				
	Hunched body posture			1	1	1										
	Sensitive to touch				1	1	1	1								
	Diarrhoea					1										
	Red staining on tray paper			1												
	Dead (total)		4	4	4	4	4	4	4	4	4	4	4	4	4	4

* Signs recorded after exposure on the day of exposure

a This sign was recorded at the late afternoon check

TABLE 5

Individual and group mean bodyweights (g)

Group	Rat	Day of observation period																			
		-5	-4	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1♂ (Control)	21	159	168	179	185	195	203	208	217	225	227	239	243	249	258	266	270	274	280	283	291
	22	157	161	170	181	189	199	204	210	218	228	236	245	253	264	272	279	289	296	301	311
	23	154	166	177	180	187	195	201	208	230	234	233	235	241	247	252	256	265	273	280	285
	24	151	163	178	180	191	198	205	212	220	225	231	244	257	267	276	282	284	293	302	307
	25	162	169	178	186	192	200	209	221	225	237	245	253	261	269	279	288	291	297	302	310
	Mean	157	165	176	182	191	199	205	214	224	230	237	244	252	261	269	275	281	288	294	301
1♀ (Control)	26	183	188	194	191	196	200	199	198	203	206	208	206	210	210	209	207	212	217	218	217
	27	174	179	184	185	191	192	193	200	199	204	208	207	208	215	220	226	230	233	239	241
	28	166	174	179	185	189	190	193	196	193	192	203	205	208	204	213	219	218	217	223	232
	29	174	177	182	190	192	199	201	201	205	211	214	215	216	221	222	224	223	227	233	235
	30	186	191	196	208	215	218	220	229	232	229	234	238	241	240	243	246	248	248	254	258
	Mean	177	182	187	192	197	200	201	205	206	208	213	214	217	218	221	224	226	228	233	237

TABLE 5

(Bodyweights - continued)

Group	Rat	Day of observation period																		
		-5	-4	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
2♂ (0.582 mg/l)	31	156	166	178	188	201	208	DEAD													
	32	154	166	178	184	193	202	DEAD													
	33	147	156	169	173	180	188	DEAD													
	34	156	163	174	182	187	196	DEAD													
	35	153	164	176	182	193	199	DEAD													
	Mean	153	163	175	182	191	199	DEAD													
2♀ (0.582 mg/l)	36	182	191	194	194	197	203	179	DEAD												
	37	173	176	182	183	192	194	DEAD													
	38	178	185	191	190	196	197	DEAD													
	39	173	179	187	190	197	201	179	DEAD												
	40	168	176	182	189	183	187	DEAD													
	Mean	175	181	187	189	193	196	179													

TABLE 5

(Bodyweights - continued)

Group	Rat	Day of observation period																			
		-5	-4	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
3♂ (0.172 mg/l)	41	155	166	176	184	195	203	178	194	206	215	226	231	242	244	261	268	276	287	295	300
	42	164	162	174	180	190	197	DEAD													
	43	153	165	173	182	191	193	195	204	208	216	222	230	241	247	258	270	275	289	293	301
	44	156	162	174	181	192	202	170	181	197	213	220	228	237	247	260	270	277	287	291	302
	45	156	165	176	185	194	203	DEAD													
	Mean	157	164	175	182	192	200	181	193	204	215	223	230	240	246	260	269	276	288	293	301
3♀ (0.172 mg/l)	46	176	178	185	191	197	191	203	200	206	207	206	220	220	219	215	219	223	225	223	228
	47	180	179	182	180	188	189	DEAD													
	48	180	179	180	175	185	189	190	185	187	190	191	192	194	195	198	199	203	212	209	209
	49	187	190	198	197	203	207	DEAD													
	50	176	177	181	184	187	191	193	198	202	204	209	207	210	207	216	219	217	222	225	230
	Mean	180	181	185	185	192	193	195	194	198	200	202	206	208	207	210	212	214	220	219	222

TABLE 5

(Bodyweights - continued)

Group	Rat	Day of observation period																			
		-5	-4	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
4♂ (0.068 mg/l)	51	168	175	181	192	201	207	215	221	226	231	242	248	251	263	269	274	287	294	305	312
	52	164	169	177	189	198	205	216	223	226	238	243	250	258	266	272	278	288	295	300	304
	53	163	169	180	186	196	203	211	219	224	239	242	250	251	266	271	283	292	298	311	315
	54	165	170	179	192	202	208	209	209	219	225	231	238	248	255	263	266	278	285	289	293
	55	174	181	190	201	212	220	222	232	240	246	255	262	275	280	293	299	312	316	326	333
	Mean	167	173	181	192	202	209	215	221	227	236	243	250	257	266	274	280	291	298	306	311
4♀ (0.068 mg/l)	56	183	189	194	199	195	202	209	212	219	214	218	220	225	222	224	228	236	231	241	246
	57	181	187	194	195	197	201	208	208	210	218	217	220	219	220	225	227	228	230	235	234
	58	182	189	191	190	194	198	203	199	201	203	204	199	203	205	210	205	214	231	233	215
	59	181	187	189	192	192	195	198	204	204	209	207	209	211	212	212	217	226	229	230	231
	60	185	190	187	188	199	197	206	210	213	218	211	216	225	227	224	228	231	232	228	231
	Mean	182	188	191	193	195	199	205	207	209	212	211	213	217	217	219	221	227	231	233	231

TABLE 5

(Bodyweights - continued)

Group	Rat	Day of observation period																		
		-5	-4	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
5♂ (0.338 mg/l)	61	154	161	171	179	187	192	DEAD													
	62	165	174	183	187	195	203	DEAD													
	63	164	173	180	190	196	204	DEAD													
	64	158	164	172	177	183	191	192	195	204	212	212	216	222	227	231	233	240	245	251	254
	65	158	162	168	174	179	184	181	181	189	198	198	205	208	215	220	224	229	231	233	235
	Mean	160	167	175	181	188	195	187	188	197	205	205	211	215	221	226	229	235	238	242	245
5♀ (0.338 mg/l)	66	181	186	187	191	190	192	174	168	166	170	185	191	194	196	200	204	208	209	215	218
	67	178	180	186	188	184	188	DEAD													
	68	179	183	183	187	195	197	DEAD													
	69	187	195	202	201	192	201	DEAD													
	70	189	194	200	200	194	200	DEAD													
	Mean	183	188	192	193	191	196	174	-	-	-	-	-	-	-	-	-	-	-	-	-

TABLE 6

Group mean daily food consumption (g/rat)

Group	Days															
	Pre-exposure					Post exposure										
	-5	-4	-3	-2	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1♂ (Control)	23	24	26	26	25	25	22	25	24	27	26	28	27	27	26	28	27	28	29
2♂ (0.582 mg/l)	21	24	25	24	24	0													
3♂ (0.172 mg/l)	24	25	24	25	24	3	21	24	25	24	27	27	27	28	28	29	31	31	31
4♂ (0.068 mg/l)	25	25	26	26	25	19	20	22	23	28	25	26	28	27	29	33	32	32	31
5♂ (0.338 mg/l)	22	22	22	23	23	6	20	21	23	22	23	22	24	22	23	24	24	22	27
1♀ (Control)	24	24	24	24	21	21	20	19	20	22	20	22	20	22	20	21	20	24	24
2♀ (0.582 mg/l)	21	24	22	21	20	0													
3♀ (0.172 mg/l)	21	23	18	21	17	10	25	18	18	19	18	20	18	19	21	20	23	21	21
4♀ (0.068 mg/l)	23	19	19	19	21	16	18	17	19	20	18	19	19	19	20	23	21	22	20
5♀ (0.338 mg/l)	22	22	20	16	21	1	3	8	16	26	24	24	23	27	25	25	26	26	28

TABLE 7

Group mean daily water consumption (g/rat)

Group	Days															
	Pre-exposure					Post exposure										
	-5	-4	-3	-2	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1♂ (Control)	26	27	29	31	50	31	32	37	35	36	39	36	41	40	37	40	39	43	41
2♂ (0.582 mg/l)	24	26	28	29	29	0													
3♂ (0.172 mg/l)	27	28	28	29	26	9	25	34	32	33	34	34	35	35	35	37	39	36	35
4♂ (0.068 mg/l)	27	30	30	32	32	30	31	31	33	34	34	33	37	34	36	40	38	39	38
5♂ (0.338 mg/l)	28	29	29	32	34	12	24	31	33	34	30	31	33	30	30	33	35	32	31
1♀ (Control)	32	36	37	36	35	35	37	30	33	39	37	35	31	37	37	40	37	43	42
2♀ (0.582 mg/l)	31	34	31	32	33	0													
3♀ (0.172 mg/l)	27	29	24	24	26	26	27	27	23	24	23	28	26	28	28	29	32	29	32
4♀ (0.068 mg/l)	30	30	28	28	31	30	29	25	28	27	31	31	30	31	33	36	35	37	32
5♀ (0.338 mg/l)	26	24	25	18	28	5	3	13	26	20	28	25	24	41	26	27	27	27	30

TABLE 8

Lung weight to bodyweight ratios

Group	Rat	Lung weight (g)	Body-weight (g)	Lung to bodyweight ratio (LW x 100/BW)	
				Survivors	Decedents
1♂ (Control)	21	1.50	291	0.52	
	22	1.63	311	0.52	
	23	1.36	285	0.48	
	24	1.47	307	0.48	
	25	1.55	310	0.50	
			Mean	0.50	
			SD	0.020	
1♀ (Control)	26	1.10	217	0.51	
	27	1.17	241	0.49	
	28	1.18	232	0.51	
	29	1.26	235	0.54	
	30	1.24	258	0.48	
			Mean	0.50	
			SD	0.022	
2♂ (0.582 mg/l)	31	2.70	208		1.30
	32	2.10	202		1.04
	33	2.00	188		1.06
	34	1.82	196		0.93
	35	1.25	199		0.63
			Mean		0.99
			SD		0.244
2♀ (0.582 mg/l)	36	1.06	179		0.59
	37	1.71	194		0.88
	38	2.16	197		1.10
	39	1.10	201		0.55
	40	1.96	187		1.05
			Mean		0.83
			SD		0.254

SD Standard deviation

TABLE 8

(Lung weight to bodyweight ratios - continued)

Group	Rat	Lung weight (g)	Body-weight (g)	Lung to bodyweight ratio (LW x 100/BW)	
				Survivors	Decedents
3♂ (0.172 mg/l)	41	1.37	300	0.46	
	42	1.42	197		0.72
	43	1.43	301	0.43	
	44	1.51	302	0.50	
	45	1.13	203		0.56
			Mean	0.48	0.64
			SD	0.022	-
3♀ (0.172 mg/l)	46	1.06	228	0.46	
	47	1.43	189		0.76
	48	1.10	209	0.53	
	49	1.70	207		0.82
	50	1.20	230	0.52	
			Mean	0.50	0.79
			SD	0.038	-
4♂ (0.068 mg/l)	51	1.52	305	0.50	
	52	1.52	300	0.51	
	53	1.91	311	0.61	
	54	1.91	289	0.66	
	55	1.85	326	0.57	
			Mean	0.57	
			SD	0.070	
4♀ (0.068 mg/l)	56	1.35	241	0.56	
	57	1.45	235	0.62	
	58	1.37	214	0.64	
	59	1.77	230	0.77	
	60	2.04	228	0.89	
			Mean	0.70	
			SD	0.135	

SD Standard deviation

TABLE 8

(Lung weight to bodyweight ratios - continued)

Group	Rat	Lung weight (g)	Body-weight (g)	Lung to bodyweight ratio (LW x 100/BW)	
				Survivors	Decedents
5♂ (0.338 mg/l)	61	1.90	192		0.99
	62	2.40	203		1.18
	63	2.30	204		1.13
	64	1.14	254	0.45	
	65	1.32	235	0.56	
			Mean	0.51	1.10
			SD	-	0.099
5♀ (0.338 mg/l)	66	1.37	218	0.63	
	67	1.35	188		0.72
	68	1.35	197		0.69
	69	1.42	201		0.71
	70	2.12	200		1.06
			Mean	-	0.80
			SD	-	0.177

SD Standard deviation

APPENDICES

Method of analysis for THIOGLYCOLIC ACID

1. Instrumentation and apparatus

Gas chromatograph:	Pye Unicam fitted with a flame ionisation detector. Pye Unicam PU 4700.
Integrator:	Spectra-Physics SP 4200.
Apparatus:	Volumetric flasks and pipettes. Diazomethane generator.

2. Reagents

Dichloroethane:	'AR' grade Fisons.
Acetic acid (glacial):	'AR' grade Fisons.
Ethanol:	James Burroughs Ltd.
Diethyl ether:	May & Baker Ltd.
Potassium hydroxide:	'AR' grade Fisons.
Diazald:	Aldrich Chemical Company.
Thioglycolic acid:	Supplied by Sponsor.

3. Preparation of sample solutions for GLC

The contents of the gas absorption traps were allowed to return to room temperature, transferred quantitatively to 25 ml volumetric flasks and diluted to volume with dichloroethane. A 4 ml aliquot of the solution was transferred to a 5 ml volumetric flask and 5 µl of acetic acid was added. Diazomethane in nitrogen(1) was passed into the solution until a permanent pale yellow colour persisted. The flask was allowed to stand for 20 minutes at room temperature and the excess diazomethane was removed by the addition of a few µl of acetic acid. The solution was diluted to 5 ml with dichloroethane.

(1) The diazomethane entrained in nitrogen was generated using a method based on that described by Schlenk and Gellerman (Anal. Chem., 32 1412 (1960)). Diazald (0.5 g) is added to a mixture of ethanol 6 ml) and ether (6 ml) contained in the diazomethane generator. 0.5 ml of 60% aqueous potassium hydroxide is added just prior to use and the diazomethane is displaced by passing a stream of nitrogen through the reaction mixture.

(Method of analysis - continued)

4. GLC

4.1. Operating conditions

Column:	2 m x 3 mm i.d. glass packed with 5% FFAP on DCLQ 80 - 100 mesh.	
Temperatures:	Column	120°C
	Injector	150°C
	Detector	150°C
Gases:	Helium (carrier)	30 ml/minute
	Hydrogen	33 ml/minute
	Air	300 ml/minute

Retention time for thioglycolic acid: 3.5 minutes.

4.2. Analysis of samples

A 3 µl aliquot of each sample solution was injected onto the GLC.

The amount of thioglycolic acid in the aliquot was evaluated using an external standard method.

The calculation was:

$$Cx = Ax/As$$

where Cx = concentration of thioglycolic acid (mg/ml)
Ax = peak area due to thioglycolic acid derivative
As = response factor (area/unit concentration for thioglycolic acid)

4.3. Standardisation

Approximately 100 mg of thioglycolic acid was accurately weighed into a 100 ml volumetric flask, dissolved in dichloroethane, and diluted to volume with dichloroethane. Volumes of 2, 4 and 8 ml of the standard solution were transferred to 10 ml volumetric flasks and diluted to 8 ml as necessary with dichloroethane. 8 ml of dichloroethane was transferred into a 10 ml volumetric flask as a reagent blank determination. 10 µl of acetic acid was added to each volumetric flask. The standard solutions were treated as in section 3 and finally diluted to 10 ml with dichloroethane.

Three 3 µl aliquots of the standard solutions were injected and the mean peak area for each standard concentration of thioglycolic acid calculated. The response factor (As) for thioglycolic acid was determined by regression analysis.

APPENDIX 2

Pathological data relating to individual rats

Group:	1	2	3	4	5
Compound:	-		THIOGLYCOLIC ACID		
Level (mg/l):	Control	0.582	0.172	0.068	0.338

Control

Rat 21♂

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

Rat 22♂

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

Rat 23♂

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

Rat 24♂

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

(Pathology - continued)

Rat 25♂

Control

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

(Pathology - continued)

Control

Rat 26♀

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

Rat 27♀

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

Rat 28♀

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

Rat 29♀

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

Rat 30♀

Control

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

0.582 mg/l

Rat 31♂ - Decedent

Macroscopic findings:

External appearance:	Wet fur around snout, jaws and eyes. Redness around snout.
Lungs:	Congested.

Microscopic findings:

Lungs:	Moderate congestion.
Liver:	No abnormalities detected.
Kidneys:	No abnormalities detected.

Rat 32♂ - Decedent

Macroscopic findings:

External appearance:	Wet fur around snout, jaws and eyes. Redness around snout.
Lungs:	Congested.

Microscopic findings:

Lungs:	Moderate congestion.
Liver:	No abnormalities detected.
Kidneys:	No abnormalities detected.

Rat 33♂ - Decedent

Macroscopic findings:

External appearance:	Wet fur around snout, jaws and eyes. Redness around snout.
Lungs:	Congested.

Microscopic findings:

Lungs:	Moderate congestion.
Liver:	No abnormalities detected.
Kidneys:	Minimal bilateral hydronephrosis.

0.582 mg/l

Rat 34♂ - Decedent

Macroscopic findings:

External appearance:	Wet fur around snout, jaws and eyes. Redness around snout.
Lungs:	Congested.

Microscopic findings:

Lungs:	Minimal congestion.
Liver:	No abnormalities detected.
Kidneys:	No abnormalities detected.

Rat 35♂ - Decedent

Macroscopic findings:

External appearance:	Wet fur around snout, jaws and eyes. Redness around snout.
Lungs:	Congested.

Microscopic findings:

Lungs:	Minimal congestion.
Liver:	No abnormalities detected.
Kidneys:	No abnormalities detected.

0.582 mg/l

Rat 36♀/

Macroscopic findings:

External appearance:	Red/brown staining around snout and jaws. Wet yellow staining around urogenital region.

Microscopic findings:

Lungs:	Minimal congestion.
Liver:	No abnormalities detected.
Kidneys:	No abnormalities detected.

Rat 37♀ - Decedent

Macroscopic findings:

External appearance:	Wet fur around snout, jaws and eyes. Redness around snout.
Lungs:	Congested.

Microscopic findings:

Lungs:	Minimal congestion.
Liver:	No abnormalities detected.
Kidneys:	No abnormalities detected.

Rat 38♀ - Decedent

Macroscopic findings:

External appearance:	Wet fur around snout, jaws and eyes. Redness around snout.
Lungs:	Congested.

Microscopic findings:

Lungs:	Minimal congestion.
Liver:	No abnormalities detected.
Kidneys:	No abnormalities detected.

/ Killed for humane reasons

(Pathology - continued)

0.582 mg/l

Rat 39♀/

Macroscopic findings:

External appearance:	Wet fur around snout, jaws and eyes.
Lungs:	Very slightly congested.

Microscopic findings:

Lungs:	Minimal congestion. Minimal dilatation of bronchiole.
Liver:	Moderate pyelitis. Moderate pelvic urothelial hyperplasia, unilateral.
Kidneys:	No abnormalities detected.

Rat 40♀ - Decedent

Macroscopic findings:

External appearance:	Wet fur around snout, jaws and eyes. Redness around snout.
Lungs:	Congested.

Microscopic findings:

Lungs:	Minimal congestion.
Liver:	No abnormalities detected.
Kidneys:	No abnormalities detected.

/ Killed for humane reasons

0.172 mg/l

Rat 41♂

Macroscopic findings:	No abnormalities detected.
Microscopic findings:	
Lungs:	No abnormalities detected.
Liver:	No abnormalities detected.
Kidneys:	Minimal unilateral hydronephrosis.

Rat 42♂ - Decedent

Macroscopic findings:	
External appearance:	Wet fur and red/brown staining around snout, jaws and eyes.
Lungs:	Congested.
Microscopic findings:	
Lungs:	Minimal congestion.
Liver:	No abnormalities detected.
Kidneys:	No abnormalities detected.

Rat 43♂

Macroscopic findings:	No abnormalities detected.
Microscopic findings:	
Lungs:	No abnormalities detected.
Liver:	No abnormalities detected.
Kidneys:	No abnormalities detected.

0.172 mg/l

Rat 44♂

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

Rat 45♂ - Decedent

Macroscopic findings:

External appearance: Wet fur and red/brown staining around snout, jaws and eyes.

Lungs: Congested.

Microscopic findings:

Lungs: Minimal congestion.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

0.172 mg/l

Rat 46♀

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

Rat 47♀ - Decedent

Macroscopic findings:

External appearance: Wet fur and red/brown staining around snout, jaws and eyes.

Lungs: Congested.

Microscopic findings:

Lungs: Minimal congestion.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

Rat 48♀

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

(Pathology - continued)

0.172 mg/l

Rat 49♀ - Decedent

Macroscopic findings:

External appearance:	Wet fur and red/brown staining around snout, jaws and eyes.
Lungs:	Congested.

Microscopic findings:

Lungs:	Minimal congestion.
Liver:	No abnormalities detected.
Kidneys:	Minimal enlargement of inner cortical tubular epithelium.

Rat 50♀

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs:	No abnormalities detected.
Liver:	No abnormalities detected.
Kidneys:	No abnormalities detected.

0.068 mg/l

Rat 51♂

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

Rat 52♂

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

Rat 53♂

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

Rat 54♂

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

(Pathology - continued)

Rat 55♂

0.068 mg/l

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

0.068 mg/l

Rat 56♀

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

Rat 57♀

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

Rat 58♀

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

Rat 59♀

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

Rat 60♀

0.068 mg/l

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: Minimal bilateral hydronephrosis.

Kidneys: No abnormalities detected.

0.338 mg/l

Rat 61♂ - Decedent

Macroscopic findings:

External appearance:	Wet fur around snout, jaws and underbody.
Lungs:	Congested.

Microscopic findings:

Lungs:	Minimal congestion.
Liver:	No abnormalities detected.
Kidneys:	No abnormalities detected.

Rat 62♂ - Decedent

Macroscopic findings:

External appearance:	Wet fur around snout, jaws and underbody, red staining around snout.
Lungs:	Congested.

Microscopic findings:

Lungs:	Minimal congestion.
Liver:	No abnormalities detected.
Kidneys:	No abnormalities detected.

Rat 63♂ - Decedent

Macroscopic findings:

External appearance:	Wet fur around snout and jaws.
Lungs:	Congested.

Microscopic findings:

Lungs:	Minimal congestion.
Liver:	No abnormalities detected.
Kidneys:	Minimal unilateral hydronephrosis.

0.338 mg/l

Rat 64♂

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

Rat 65♂

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

0.338 mg/l

Rat 66♀

Macroscopic findings: No abnormalities detected.

Microscopic findings:

Lungs: No abnormalities detected.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

Rat 67♀ - Decedent

Macroscopic findings:

External appearance: Wet fur around snout, jaws and eyes.

Lungs: No abnormalities detected.

Microscopic findings:

Lungs: Minimal congestion.

Liver: No abnormalities detected.

Kidneys: No abnormalities detected.

Rat 68♀ - Decedent

Macroscopic findings:

External appearance: Wet fur around snout, jaws, eyes and urogenital area.

Lungs: No abnormalities detected.

Microscopic findings:

Lungs: Minimal congestion.

Liver: No abnormalities detected.

Kidneys: Minimal enlargement of inner cortical tubular epithelium.

0.338 mg/l

Rat 69♀ - Decedent

Macroscopic findings:

External appearance:	Wet fur around snout, jaws, eyes and urogenital area.
Lungs:	Slight congestion.

Microscopic findings:

Lungs:	Minimal congestion.
Liver:	No abnormalities detected.
Kidneys:	No abnormalities detected.

Rat 70♀ - Decedent

Macroscopic findings:

External appearance:	Wet fur around snout, jaws and urogenital area.
Lungs:	Congestion.

Microscopic findings:

Lungs:	Minimal congestion.
Liver:	No abnormalities detected.
Kidneys:	No abnormalities detected.

We the undersigned, hereby declare that the work was performed under our supervision according to the procedures herein described, and that this report provides a correct and faithful record of the results obtained.

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Director of Research and Principal Pathologist

COMPLIANCE WITH GOOD LABORATORY PRACTICE STANDARDS

To the best of my knowledge and belief the study described in this report was conducted in compliance with the following Good Laboratory Practice Standards:

United States Environmental Protection Agency,
Title 40 Code of Federal Regulations Part 792,
Federal Register, 29 November 1983

Organization for Economic Co-operation and Development
ISBN 92-64-12367-9, Paris 1982

Good Laboratory Practice, The United Kingdom Compliance
Programme, Department of Health & Social Security 1986

G. C. Jackson

Graham C. Jackson, B.A., L.R.S.C.,
Study Director

13/1/89
Date

QUALITY ASSURANCE STATEMENT

Certain studies of short duration, such as that described in this report, are conducted at HRC in a setting which involves frequent repetition of similar or identical procedures. At or about the time the study described in this report was in progress, 'process-based' inspections were made by the Quality Assurance Department of critical procedures relevant to this study type. For the inspection of any given procedure, at least one study was selected without bias. The findings of these inspections were reported promptly to the Study Director and to HRC management.

This report has been audited by the HRC Quality Assurance Department. It is considered to be an accurate presentation of the procedures and practices employed during the course of the study and an accurate presentation of the findings.

P. H. C. Richold

Peter H.C.V. Richold, B.Sc.,
Systems Compliance Auditor,
Quality Assurance Department.

11.1.89
Date

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MAR 30 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests".

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EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure 12988A

Triage of 8(e) Submissions

Date sent to triage: _____

(NON-CAP) CAR

Submission number: 12988A

TSCA Inventory: (Y) N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

(ATOX) SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX CTOX EPI RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.): _____

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CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 0994 - 12988 SEQ. A

TYPE: (INT) SUPP FLWP

SUBMITTER NAME: EIF Atochem North America, Inc

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL. ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS
0401 NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF INTENT TO SUBMIT
(0404) LABELING/MSDS CHANGES
0405 PROCESS/LANDFILL CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 09/15/94 [redacted] DATE: 09/28/94 CSRAD DATE: 11/18/94

CHEMICAL NAME:

CAS#
68-11-1

INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04	0216	EPI/CLIN	01 02 04	0241	IMMUNO (ANIMAL)	01 02 04
0202	ONCO (ANIMAL)	01 02 04	0217	HUMAN EXPOS (PROD CONTAM)	01 02 04	0242	IMMUNO (HUMAN)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04	0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04	(0243)	CHEM/PHYS PROP	01 02 04
0204	MUTA (IN VITRO)	01 02 04	0219	HUMAN EXPOS (MONITORING)	01 02 04	0244	CLASTO (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04	0220	ECO/AQUA TOX	01 02 04	0245	CLASTO (ANIMAL)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04	0221	ENV. OCCC/REL/FATE	01 02 04	0246	CLASTO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04	0222	EMER INCI OF ENV CONTAM	01 02 04	0247	DNA DAM/REPAIR	01 02 04
0208	NEURO (HUMAN)	01 02 04	0223	RESPONSE REQEST DELAY	01 02 04	0248	PROD/USE/PROC	01 02 04
0209	NEURO (ANIMAL)	01 02 04	0224	PROD/COMP/CHEM ID	01 02 04	0251	MSDS	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04	0225	REPORTING RATIONALE	01 02 04	0299	OTHER	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04	0226	CONFIDENTIAL	01 02 04			
(0212)	ACUTE TOX. (ANIMAL)	01 (02) 04	0227	ALLERG (HUMAN)	01 02 04			
0213	SUB ACUTE TOX (ANIMAL)	01 02 04	0228	ALLERG (ANIMAL)	01 02 04			
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04	0239	METAB/PHARMACO (ANIMAL)	01 02 04			
0215	CHRONIC TOX (ANIMAL)	01 02 04	0240	METAB/PHARMACO (HUMAN)	01 02 04			

TRIAGE DATA:	NON-CBI INVENTORY	ONGOING REVIEW	SPECIES	TOXICOLOGICAL CONCERN:	USE:	PRODUCTION:
	(YES)	YES (DROP/REFER)	RAT	LOW		
CAS SR	NO	NO (CONTINUE)		(MED) Acute Inhalation Toxicity		
	IN TRIAGE	REFER		HIGH		

V: [redacted]

12988A

M

Acute inhalation toxicity is of medium concern based on an estimated 4 hour LC_{50} of 0.21 g/m^3 in rats (5/sex/dose). Mortality and corresponding doses (g/m^3) were 0/10 (0.068), 4/10 (0.172), 7/10 (0.338) and 10/10 (0.582). Clinical signs included nasal irritation, abnormal respiration, restlessness and hunched posture (all doses). Congested lungs were observed in the decedents.